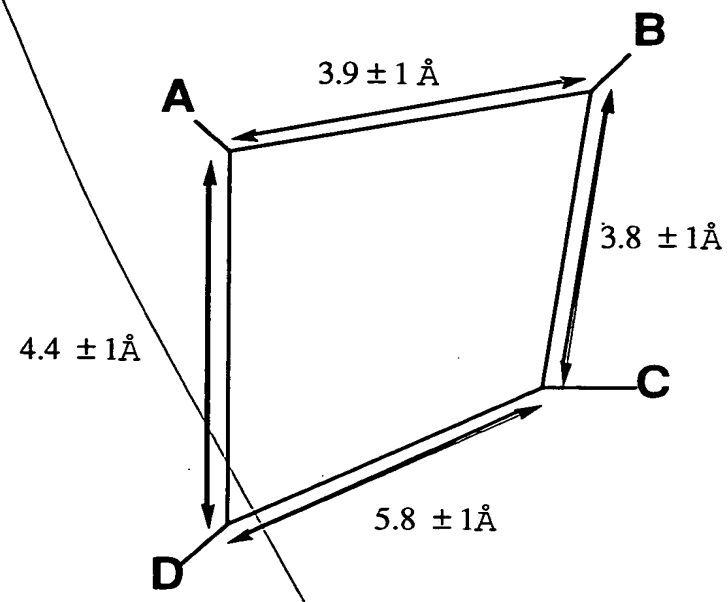
CLAIMS:

1. A compound which is an antagonist of a G protein-coupled receptor, which has no agonist activity, and which has a cyclic on constrained acyclic structure adapted to provide a framework of approximate dimensions as set out in Structure I:

Structure I



where the numerals refer to distances between C_α carbons of amino acids or their analogues or derivatives, and A, B, C and D are not necessarily on adjacent amino acids, or analogues or derivatives thereof; and

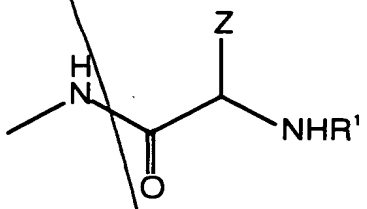
where the critical amino acid side chains are designated by A, B, C and D, where

A is any common or uncommon, basic, charged amino acid side chain which serves to position a positively charged group in this position;

B is any common or uncommon, aromatic amino acid side chain which serves to position an aromatic side-chain in this position;

C is any common or uncommon, hydrophobic amino acid side chain which serves to position any alkyl, aromatic or other group in this position;

D is any common or uncommon, aromatic amino acid which serves to position an aromatic side-chain in this position, and has the structure:



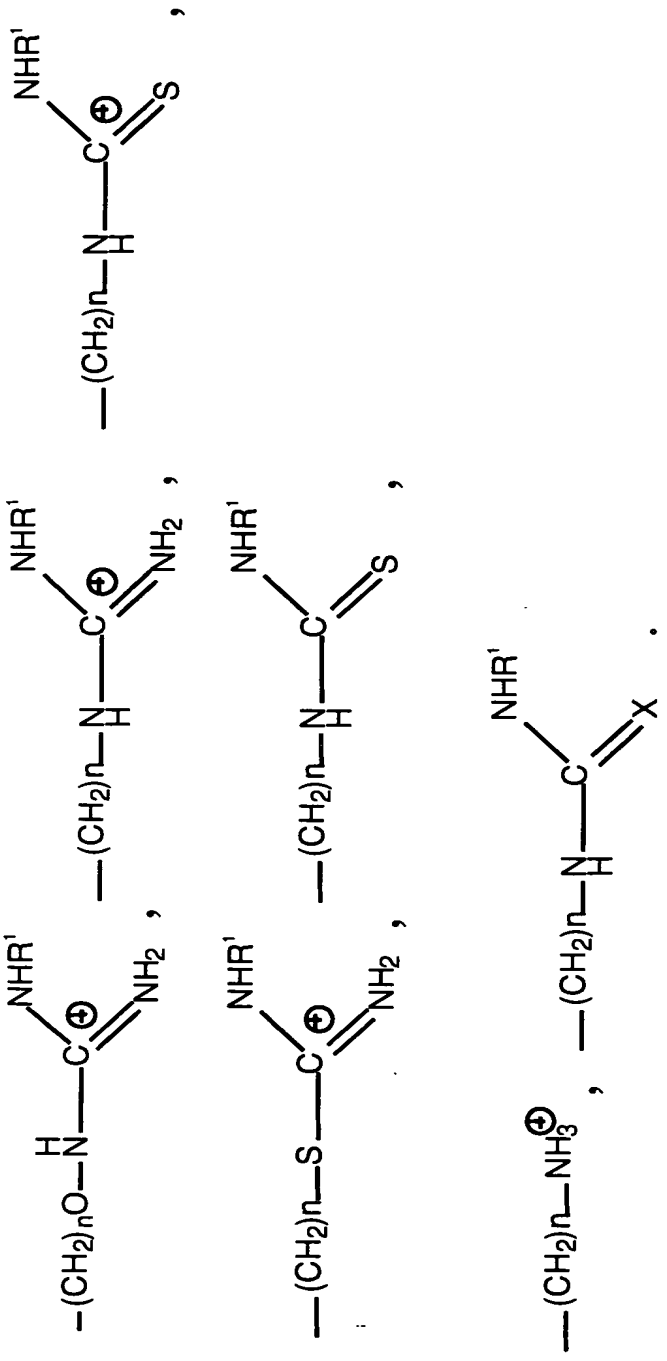
where Z is indole, indole methyl, benzyl, benzene, naphthyl, naphthyl methyl, or a derivative thereof; and

R^1 is H or an alkyl, aromatic, acyl or aromatic-acyl group.

2. An antagonist according to Claim 1, in which the G protein-coupled receptor is the C5a receptor.

3. An antagonist according to Claim 1 ~~or Claim 2~~, in which

A is one of the following side-chains



or another mimetic of an arginine side chain;

where

X is NCN, NNO_2, $CHNO_2$ or NSO_2NH_2;

n is an integer from 1 to 4, and

R^1 is H or an alkyl, aryl, CN, NH_2, OH, $-CO-CH_2CH_3$, $-CO-CH_3$, $-CO-CH_2CH_2CH_3$, $-CO-CH_2Ph$, or -CO-Ph;

B is an indole, indole methyl, benzyl, phenyl, naphthyl, naphthyl methyl, cinnamyl group, or any other derivative of the aromatic group; and

C is D- or L-cyclohexylalanine (Cha), leucine, valine, isoleucine, phenylalanine, tryptophan or methionine.

4. An antagonist according to Claim ~~3~~ 1, in which R^1 is methyl, ethyl, propyl, or butyl.

5. An antagonist according to ~~any one of Claims 1~~ Claim 1 to 4, which is a constrained acyclic compound, and comprises a type II β-turn.

6. An antagonist according to Claim 5, in which the type II β-turn comprises a γ-turn within the type II β-turn.

7. An antagonist according to ~~any one of claims 1~~ Claim 1 to 4, which is a cyclic peptide or peptide derivative.

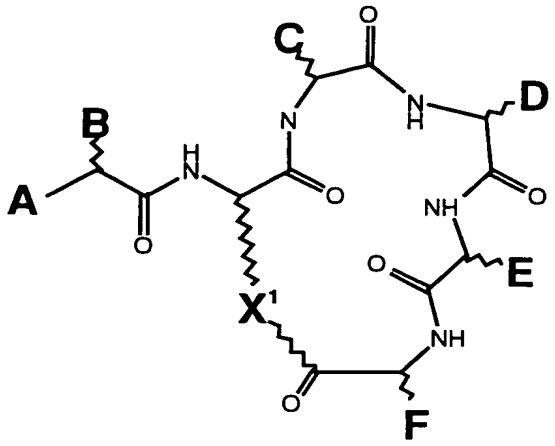
8. An antagonist according to ~~any one of Claims 1~~ Claim 1 to 4, of formula

Ac-phe-[lys-pro-(dCha)-trp-arg] or
Ac-phe-[orn-pro-(dCha)-trp-arg]

9. An antagonist according to ~~any one of Claims 1~~ Claim 1 to 7 in which A is L-arginine.

10. An antagonist according to Claim 1, which has antagonist activity against C5aR, has no agonist activity against C5a, and has the general formula:

Structure II



where A is H, alkyl, aryl, NH_2, NHalkyl, $N(alkyl)_2$, NHaryl or NHacyl;

B is an alkyl, aryl, phenyl, benzyl, naphthyl or indole group, or the side chain of a D- or L-amino acid selected from the group consisting of phenylalanine, homophenylalanine, tryptophan, homotryptophan, tyrosine, and homotyrosine;

C is the side chain of a D-, L- or homo-amino acid selected from the group consisting of proline, alanine, leucine, valine, isoleucine, arginine, histidine, aspartate, glutamate, glutamine, asparagine, lysine, tyrosine, phenylalanine, cyclohexylalanine, norleucine, tryptophan, cysteine and methionine;

D is the side chain of a D- or L-amino acid selected from the group consisting of cyclohexylalanine, homocyclohexylalanine, leucine, norleucine, homoleucine, homonorleucine and tryptophan;

E is the side chain of a D- or L-amino acid selected from the group consisting of tryptophan and homotryptophan;

F is the side chain of a D- or L-amino acid selected from the group consisting of arginine, homoarginine, lysine and homolysine; and

X^1 is $-(CH_2)_nNH-$ or $(CH_2)_n-S-$, $-(CH_2)_2O-$, $-(CH_2)_3O-$, $-(CH_2)_3-$, $-(CH_2)_4-$, or $-CH_2COCHRNH-$, where R is the side chain of any common or uncommon amino acid, and

where n is an integer of from 1 to 4,

11. An antagonist according to Claim 10, in which F is a L-amino acid.

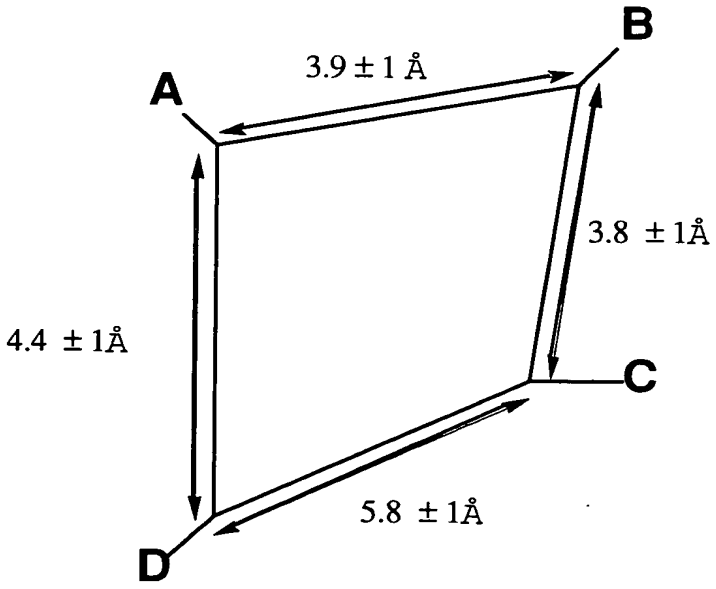
12. An antagonist according to Claim 11, in which F is L-arginine.

13. An antagonist according to ~~any one of Claims 10 to 12~~ Claim 10, selected from the group consisting of compounds **11**, **12**, **13**, **14**, **15**, **16**, **17**, **18**, **19**, **20**, **21**, **22**, **23**, **24**, **25**, **26**, **27** and **28**.

14. An antagonist according to ~~any one of Claims 3 and 10 to 13~~ Claim 13, in which n is 2 or 3.

15. A compound which is an agonist of a G protein-coupled receptor, and which has structure III

Structure III



where the numerals refer to distances between C_α carbons of amino acids or their analogues or derivatives,

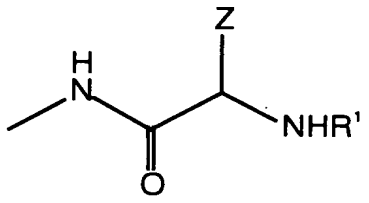
and A, B, C and D are not necessarily on adjacent amino acids, or analogues or derivatives thereof; and

where B is a non-aromatic amino acid, and

A is any common or uncommon, basic, charged amino acid side chain which serves to position a positively charged group in this position;

C is any common or uncommon, hydrophobic amino acid side chain which serves to position any alkyl, aromatic or other group in this position; and

D is any common or uncommon, aromatic amino acid which serve to position an aromatic side-chain in this position, and has the structure:



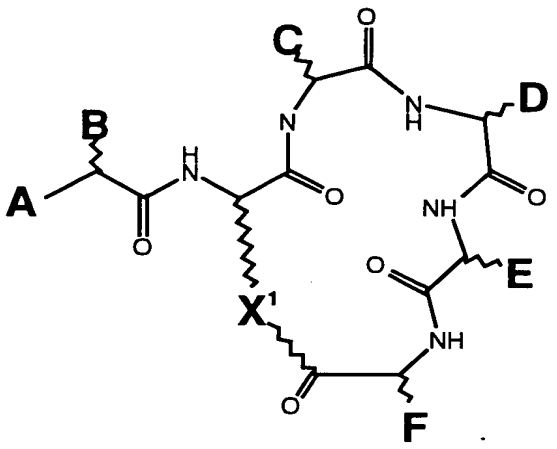
where Z is indole, indole methyl, benzyl, benzene, naphthyl, naphthyl methyl, or a derivative thereof; and

R is H or an alkyl, aromatic, acyl or aromatic-acyl group.

16. A compound according to Claim 15, where B is the D- or L-form of alanine, leucine, valine, norleucine, glutamic acid, aspartic acid, methionine, cysteine, isoleucine, serine or threonine.

17. A compound according to Claim 15 ~~or Claim 16~~, in which the compound is of structure IV,

Structure IV

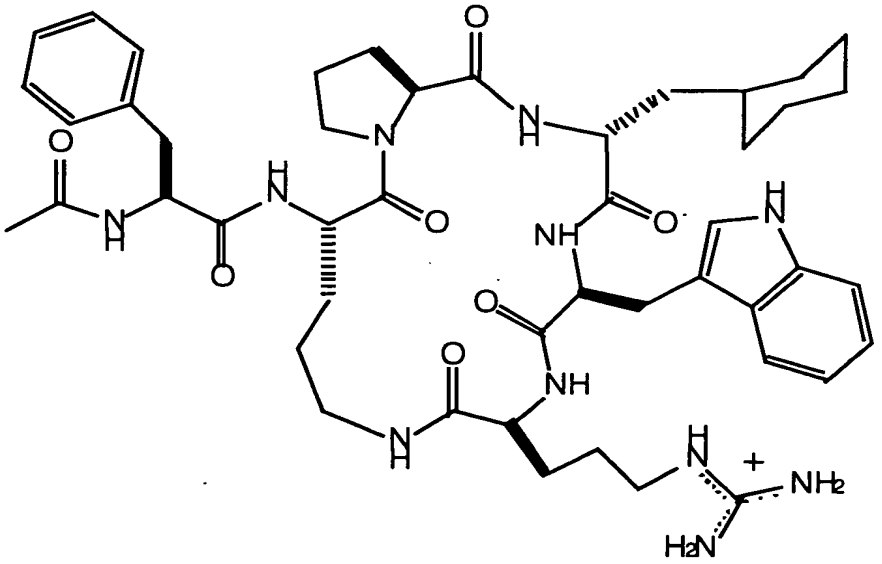


where E is any amino acid other than tryptophan and homotryptophan, and

F is the side chain of a D- or L-amino acid selected from the group consisting of arginine, homoarginine, lysine and homolysine.

18. A compound according to ~~any one of Claims 15 to 17~~ Claim 15, wherein the compound is an agonist of C5a.

19. A compound according to Claim 10, of structure



20. A composition comprising a compound according to ~~any one of Claims 1 to 19~~, together with a pharmaceutically-acceptable carrier or excipient.

21. A method of treatment of a pathological condition mediated by a G protein-coupled receptor, comprising the step of administering an effective amount of a compound according to ~~any one of Claims 1 to 19~~, to a mammal in need of such treatment.

22. A method according to Claim 21, wherein the condition mediated by a G protein-coupled receptor involves overexpression or underregulation of C5a.

23. A method according to Claim 21, wherein the condition is selected from the group consisting of rheumatoid arthritis, adult respiratory distress syndrome (ARDS), systemic lupus erythematosus, tissue graft rejection, ischaemic heart disease, reperfusion injury, septic shock, psoriasis, gingivitis, atherosclerosis, Alzheimer's disease, multiple sclerosis, lung injury and extracorporeal post-dialysis syndrome.

24. Use of a compound according to any one of Claims 1 to 19 in treatment of a pathological condition mediated by a G protein-coupled receptor.

25. Use according to Claim 24, in which the condition is mediated by C5a.

26. Use according to Claim 25, in which the condition mediated by G protein-coupled receptors involves overexpression or underregulation of C5a.

27. Use according to any one of Claims 24 to 26, in which the condition is selected from the group consisting of rheumatoid arthritis, adult respiratory distress syndrome (ARDS), systemic lupus erythematosus, tissue graft rejection, ischaemic heart disease, reperfusion injury, septic shock, psoriasis, gingivitis, atherosclerosis, Alzheimer's disease, multiple sclerosis, lung injury and extracorporeal post-dialysis syndrome.

28. Use of a compound according to any one of Claims 1 to 19 in the manufacture of a medicament for the

treatment of a condition mediated by a G protein-coupled receptor.

29. Use according to Claim 28, in which the condition is mediated by C5a.

30. Use according to Claim 29, in which the condition mediated by G protein-coupled receptors involves overexpression or underregulation of C5a.

31. A compound according to Claim 1, substantially as hereinbefore described with reference to the examples and drawings.

32. A method according to Claim 21, substantially as hereinbefore defined with reference to the examples and drawings.